REMARKS

I Status of the Application

Claims 1-54 were originally filed in the present application. In response to the Restriction Requirement mailed May 25, 2006, Applicants elected to prosecute the claims of Group III, drawn to a method of decolonizing skin pathogen populations.

Applicants have amended the specification to correct informalities regarding usage of trademarks. Applicants note that trademarks were capitalized throughout the specification, but now also include generic terminology.[1]

Applicants also herein amend Claims 34, 37, 38, 44 and 45. Claims 37 and 45 have been amended to correct informalities present therein. In particular, Claim 37 has been amended to recite "ethylenediaminetetraacetic acid" in place of "EDTA" and Claim 45 has been amended to reference common chemical names in place of trademark names. Support for the amendments can be found throughout the specification, for example, in paragraph 34 (Claim 34), paragraph 38 (Claim 38), and paragraph 56 (Claim 44), among other places.

As such, Claims 33-46 and 55-75 are pending in the application.

II. The Claims Are Enabled and Distinctly Claim the Invention

Applicants note that any amendments or cancellation of claims are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),[2] and without waiving the right to prosecute the cancelled claims (or similar claims) in the future.

The Examiner rejected Claims 33-46 and 55-75 under 35 U.S.C. §112, first paragraph, as allegedly not being enabled. Applicants respectfully disagree.

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[1] According to MPEP 608.01(v)(l), "Trademarks should be identified by capitalizing each letter of the mark (in the case of word or letter marks) or otherwise indicating the description of the mark (in the case of marks in the form of a symbol or device or other nontextual form). Every effort should be made to prevent their use in any manner which might adversely affect their validity as trademarks." Applicants point out that there is no separate requirement that a trademark symbol follow the capitalized trademark.

[2] 65 Fed. Reg. 54603 (Sept., 8, 2000).

The Specification fully describes and enables a method of decolonizing bacterial populations comprising topically applying to a patient in need thereof at a bacterially infected site a topical composition comprising lysostaphin and one or more lantibiotics (Claim 1).[3] The Examiner acknowledges that "The specification enables the use of wild-type lysostaphin and nisin in a method of decolonizing bacterial populations."[4]

The Examiner alleges that the "specification does not enable any person skilled in the art to which it pertains...to make and use the invention commensurate in scope with these claims."[5] Applicants respectfully disagree.

Nonetheless, Applicants have amended the claims. In particular, Applicants have amended Claim 34 to recite the types of lysostaphin being claimed to include wild-type lysostaphin, recombinant lysostaphin and a lysostaphin mutant that lacks the first two alanine amino acids of the full length lysostaphin amino acid sequence. The specification provides clear support for these newly added limitations, for example, in the Examples and in paragraph 34. For example, the Specification incorporates by reference WO 03/082124 that describes in detail a recombinant lysostaphin mutant that lacks the first two alanine amino acids of the full length lysostaphin amino acid sequence. One of ordinary skill in the art could easily utilize the described mutant in a method of the present invention without undue experimentation.

Similarly, Applicants have amended Claim 38 to recite specific nisin mutants (H27K and H31K) described in the Specification (e.g., in paragraph 38) and known to one of ordinary skill in the art.

Accordingly, Applicants respectfully request that the rejection of Claims 33-46 and 55-75 under 35 U.S.C. §112 first paragraph be withdrawn.

The Examiner also rejected Claims 34, 38, 44, 45 and 63 under 35 U.S.C. §112 second paragraph as allegedly failing to particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully disagree.

Nonetheless, Applicants have amended each of these claims.

Amendments to Claims 34 and 38 are described above.

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[3] See, e.g., Examples 1-6 on pages 32-40.
[4] Office Action at page 3.
[5] Office Action at page 3.

Applicants have amended Claim 44 to recite "glycerides of fatty acids" described in the Specification (e.g., in paragraph 56).

Applicants have amended Claim 45 to recite common chemical names rather than trademark language.

With regard to Claim 63, Applicants point out that the term "partial fatty acid" does not appear in the original Claim. Rather the term "hard fat" appears. Applicants respectfully submit that the specification clearly defines "hard fat" as "a fatty acid triglyceride blend that is solid at room temperature" (e.g., in paragraph 54). Applicants have amended Claim 63 to recite this language.

It is respectfully submitted that the amended claims particularly point out and distinctly claim the invention. Applicants respectfully request that the rejection under 35 U.S.C. §112 second paragraph be withdrawn.

III. The Claims are Not Anticipated

The Examiner rejected Claims 33-37, 39-40, 42-44, 46, 56-61 and 63-75 under 35 U.S.C. § 102(b) as alleged being anticipated by Blackburn et al. (U.S. Pat. No. 5,762,948, hereinafter "the '948 patent"). Applicants respectfully disagree.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."[6] Furthermore, the disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient if it cannot be produced without undue experimentation.[7] A prior art reference provides an enabling disclosure only "if the public was in possession of the claimed invention before the date of invention."[8]

The Examiner alleges that "Blackburn et al. [the '948 patent] teach a method of disinfecting (decolonizing) bacterial populations comprising topically applying to a patient a topical composition comprising nisin and one or more lantibiotics such as

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[6] *Verdegaal Bros. v Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987), and MPEP 2131.
[7] See MPEP 2121.01, citing *Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research*, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003)
[8] See MPEP 2121.01.

lysostaphin (the Abstract, column 3 and columns 11-12, Example 7)." This allegation is legally and factually unsupportable.

The '948 patent does not teach or suggest that lysostaphin is a lantibiotic (i.e., a lanthionine-containing bacteriocin such as nisin). In fact, lysostaphin is not a lantibiotic.[9] The Examiner's allegation that the Abstract, column 3 and columns 11-12 and Example 7 anticipate the claims is simply incorrect. Applicants respectfully submit that the Examiner has mistakenly interpreted lysostaphin to be a lantibiotic, which it is not, leading to the erroneous conclusion that the '948 patent anticipates the claims.

The '948 patent does not teach a method of decolonizing bacterial populations comprising topically applying to a patient in need thereof at a bacterially infected site a topical composition comprising lysostaphin **and** one or more lantibiotics (of Claim 33). Indeed, no evidence has been cited to support such a teaching. This is not surprising as the '948 patent does not provide any type of protocol for generating a composition comprising lysostaphin **and** one or more lantibiotics **nor how or if** such a composition could be used to decolonize bacteria present at an infected site of a patient. Thus, the Examiner fails to cite to evidence within the '948 patent, or from any source, that would allow one of ordinary skill in the art background sufficient to practice the instant invention. The '948 patent does not place the public in possession of the claimed invention.

Accordingly, because the '948 patent does not teach or enable a method of applying to a patient a composition comprising a combination of lysostaphin and one or more lantibiotics, the '948 patent does not anticipate Claim 33.

Applicants respectfully submit that because Claim 33 is not anticipated, claims dependent thereon (i.e., Claims 34-37, 39-40, 42-44, 46, 56-61 and 63-75) are also not anticipated.

Applicants respectfully request that this rejection be withdrawn.

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[9] Lysostaphin is a 27-kDa endopeptidase produced by *Staphylococcus simulans* that is capable of specifically cleaving the cross-linking pentaglycine bridges in the cell walls of staphylococci (See, e.g., Quickel et al.,1971. Appl. Microbiol. 22:446-450). Lysostaphin is not a lanthionine containing bacteriocin.

III. The Claims are Not Obvious

In the Office Action mailed September 25, 2006, the Examiner rejected Claims 33-37, 39-40, 42-44, 46, 55-75 under 35 U.S.C. §103(a) as allegedly being unpatentable over Daley et al. (U.S. Pat. No. 5,342,612, hereinafter "the '612 patent") in view of Blackburn et al. (U.S. Pat. No. 4,980,163, hereinafter "the '163 patent"). Applicants respectfully disagree.

In rejecting claims under 35 U.S.C. § 103, the Examiner bears the initial burden of presenting a prima facie case of obviousness.[10] A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art.[11] An obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art.[12]

Applicants respectfully submit that the cited references, individually or combined, do not suggest how to modify compositions and methods disclosed therein in order to produce the claimed invention, and the cited references do not provide a reasonable expectation of success for carrying out the claimed invention.

A) The '612 and '163 patents

The '612 patent describes compositions comprising lysostaphin in various aqueous surfactant vehicles (e.g., saline, PLURONIC F127, glycerol, poloxamer 407 NF, triacetin, and peanut oil) to potentially produce a lysostaphin with enhanced biological activity and methods of using the composition to enhance lysostaphin bacteriostatic and/or bactericidal efficacy against *S. aureus* .[13] Furthermore, the '162 patent shows that

> "Lysostaphin formulated in poloxamer 407 NF elicits the best cure rate with 57% cures, and an average of 9.6 clear milkings of relapsed quarters. This represents a 2-3 fold improvement of the therapeutic efficacy of lysostaphin formulated in saline. Neither glycerol nor triacetin (both have a cure rate of 25%) has any significant effect on potentiating the in vivo efficacy of lysostaphin. Lysostaphin in a similar formulation to CEFA-LAK (peanut oil base) cures 0% of the treated quarters."[14]

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[10] See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993).
[11] In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993).
[12] In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).
[13] See U.S. Pat. No. 5,342,612, Examples 3-5and 9-10.
[14] See U.S. Pat. No. 5,342,612, column 13, lines 25-35.

Thus, some of the aqueous surfactant vehicles had no effect on lysostaphin bacteriostatic and/or bactericidal efficacy, some enhanced it, and some negated it altogether.
In addition, the '612 patent provides a laundry list of antimicrobial agents that may also benefit from combination with an aqueous surfactant vehicle including a bacteriolytic peptide such as an enzyme or bacteriostatic peptide, for example, lysostaphin, lysozyme, nisin, magainins ...or may be formulated with antibiotics such as amoxicillin, ampicillin, cephapirin, cloxacillin, hetacillin, penicillin G, etc.[15] No protocol for generating a composition comprising nisin with an aqueous surfactant vehicle nor data suggesting how nisin antimicrobial activity might be altered by such a vehicle is provided.

The '163 patent describes bacteriocin compositions comprising lysostaphin and nisin that have enhanced bactericidal activity (compared to either used individually) toward *S. aureus* or *S. agalactiae* co-incubated with the bacteriocin composition in milk for two hours at 37° C.[16]

The Examiner alleges that it would be prima facie obvious at the time the invention was made to modify the method of eliminating bacterial infections as taught by the '612 patent to administer to a patient with a bacterial infection because the '163 patent discloses that a composition comprising lysostaphin and nisin provide broad range bactericidal activity against bacterial infections.[17] (Office Action at page 4). Applicants respectfully disagree.

The cited references, individually or in combination, do not teach or disclose a method of decolonizing bacterial populations comprising topically applying to a patient in need thereof at a bacterially infected site a topical composition comprising lysostaphin and one or more lantibiotics. For example, the cited references do not provide any type of administration protocol for how a composition comprising lysostaphin and a lantibiotic could be topically administered to an infected site nor whether such administration would be effective at decolonizing bacterial populations present within an infected site. Furthermore, no guidance is provided by either reference as to whether a topical composition comprising lysostaphin, nisin and a surfactant, or a chelating agent or

[15] See U.S. Pat. No. 5,342,612, columns 3 and 4, lines 30-40 and 4-15, respectively.
[16] See U.S. Pat. No. 4,980,163 Examples 1 and 2.
[17] Office Action at page 4.

carvacol would be effective at decolonizing bacterial populations present within an infected site. Similarly, no guidance is provided by either reference as to whether a topical composition comprising lysostaphin, nisin and an oil-in-water emulsion based cream or lotion comprising an aqueous phase, an oil phase and an emulsifier would be effective at decolonizing bacterial populations present within an infected site, nor is any guidance provided regarding the number of applications of a topical composition comprising lysostaphin and a lantibiotic that would be effective at decolonizing bacterial populations present within an infected site of a patient.

Indeed, the cited references actually teach that addition of various reagents to a composition comprising lysostaphin and nisin can inhibit their bactericidal properties. For example, the '162 patent teaches that lysostaphin in an oil base (peanut oil base) loses its bactericidal capacity and that EDTA can inhibit the activity of nisin.

Thus, one of ordinary skill in the art would have no reasonable expectation of success that a topical composition comprising lysostaphin and one or more lantibiotics could be used successfully to decolonizing bacterial populations present within a bacterially infected site of a patient. There exists no clear direction or guidance provided by the cited references, individually or combined, rendering obvious to one skilled in the art the ability to use a composition comprising lysostaphin and a lantibiotic to decolonizing bacterial populations present within a bacterially infected site of a patient.

Applicants submit, for the sake of argument, that even if the references provide a generalized teaching to try to use a composition comprising lysostaphin and a lantibiotic to decolonizing bacterial populations present within a bacterially infected site of a patient, that this is nothing more than an invitation to experiment and does not render obvious Applicants' invention.

In discussing obviousness in In re O'Farrell, 853 F.2d 894, 903-04, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)(citations omitted) the Federal Circuit stated:

> "The admonition that 'obvious to try' is not the standard under § 103 has been directed mainly at two kinds of error. In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. . . . In others, what

> was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it."

Applicants respectfully submit that the Examiner has not established a prima facie case of obviousness due to the inability to provide references, alone or in combination, that render obvious to one skilled in the art the use of a composition comprising lysostaphin and a lantibiotic to decolonizing bacterial populations present within a bacterially infected site of a patient. At best, the Examiner has provided evidence that it would be obvious to experiment or try administration of a composition comprising lysostaphin and a lantibiotic to decolonizing bacterial populations present within a bacterially infected site of a patient..

However, "obvious to experiment" is not the standard for obviousness.[18] The Federal Circuit has made very clear that one must determine whether "the prior art would have suggested to one of ordinary skill in the art that this process **should** be carried out and **would** have a reasonable likelihood of success, viewed in light of the prior art." *Id.* at 1531 (Emphasis added). There is no reasonable expectation of success because there was no way to predict whether a composition comprising lysostaphin and a lantibiotic could be used to decolonize bacterial populations present within a bacterially infected site of a patient. Applicants respectfully submit that the Examiner has improperly applied an "obvious to experiment" standard.

Thus, the Examiner has neither established that the cited references suggest the claimed subject matter nor revealed a reasonable expectation of success to one reasonably skilled in the art.

Accordingly, Applicants respectfully request that the rejection of Claims 33-37, 39-40, 42-44, 46, 55-75 under 35 U.S.C. §103(a) be withdrawn.

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[18] *In re Dow Chemical*, 5 USPQ2d 1529, at 1532 (Fed. Cir. 1988).

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicants have addressed all grounds for rejection and Applicants' claims should be passed to allowance. Reconsideration of the application is respectfully requested. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourages the Examiner to call the undersigned collect at (608) 218-6900.

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